set forth in 37 C.F.R. §§ 1.821(a)(1) and (a)(2). The Examiner therefore stated that the application fails to comply with the requirements of 37 C.F.R. §§ 1.821 - 1.825, and that applicants must comply with these rules as set forth in the Notice.

Specifically, the Examiner required applicants to provide 1) a computer readable form (C.R.F.) copy of the "Sequence Listing"; 2) a paper copy of the "Sequence Listing", and 3) a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter.

In response, applicants submit herewith a computer readable form (C.R.F.) of the "Sequence listing" in ASCII (DOS) format on the enclosed computer diskette.

Applicants further submit a paper copy of the Sequence Listing, attached herewith as **Exhibit B**, and a Statement of Compliance Under 37 C.F.R. §1.821(f) attached hereto as **Exhibit C**, certifying that the computer readable form as required by 37 C.F.R. §1.821(e) is identical to the paper copy of the Sequence Listing attached as **Exhibit B**. Applicants believe that the enclosed C.R.F., paper copy of the Sequence Listing (**Exhibit B**) and Statement of Compliance Under 37 C.F.R. §1.821(f)) (**Exhibit C**) now fully comply with the requirements of §1.821 through §1.825.

If a telephone interview would be of assistance in advancing the prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee, except for the $155.00 fee for a two-month extension of time, is deemed necessary in connection with the filing of this Amendment. If any additional fees are required, authorization is hereby given to charge the amount of such fees to Deposit Account No. 03-3125.

Respectfully submitted,

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:

Assistant Commissioner for Patents
Washington, D.C. 20231.

9/25/01
Alan J. Morrison Date
Reg. No. 37,399

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Marked Versions Of Amended Paragraphs:

(Amended) **Construction of the subtraction library and preliminary sequencing**. PolyA+ RNA was isolated from the fifth passage synoviocytes using a mRNA Isolation Kit (Stratagene). 2ug of twice purified polyA+ RNA was used as a template for cDNA synthesis in the RiboClone cDNA Synthesis System (Promega). The synthesized cDNA was ligated with the oligonucleotides GATCCGCGGCCGC (SEQ ID NO:1) and GCGGCCGCGT (SEQ ID NO:2) as described(Hubank 1994). After selection of fragments larger than 250 nucleotides by fractionation through a Sephacryl S-400 column (Pharmacia) and phosphorylation with T4 polynucleotide kinase, the cDNA was digested with the restriction enzyme MboI. The fragments were then ligated with oligonucleotides J-Bam-24 ACCGACGTCGACTATCCATGAACG (SEQ ID NO:3) and J-Bam-12 GATCCGTTCATG (SEQ ID NO:4), and amplified as described (Hubank 1994). The PCR products, after fractionation through Sephacryl S-400 column, were digested with MboI and they comprised the primary amplicon. DNA from rheumatoid arthritis synoviocytes was further ligated with oligonucleotides N-Bam-24 AGGCAACTGTGCTATCCGAGGGAG (SEQ ID NO:5) and N-Bam-12 GATCCTCCCTCG (SEQ ID NO:6). The hybridization was performed as described(26) except that the ratio of tester and driver was kept 1:100 throughout. 10ug of the osteoarthritis primary amplicon were hybridized with 0.1ug of the rheumatoid arthritis primary amplicon in 5ul of 24mM EPPS,pH8.0, 1mM EDTA, 1M NaCl for 20hr at 67C. The hybridized DNA was subjected to 10 cycles of PCR with N-Bam-24 as a primer, followed by digestion with mung bean nuclease. One four hundredth of the digests was further amplified for 20 cycles. After digestion with MboI, the DNA product was ligated with oligonucleotides R-Bam-24 AGCACTCTCCAGCCTCTCACCGAG (SEQ ID NO: 7) and R-Bam-12 GATCCTCGGTGA (SEQ ID NO:8). Hybridization and amplification steps were repeated. After redigestion with MboI, the resulting differentially subtracted cDNA fragments were cloned

into a BamHI site of the plasmid pUC18. The recombinants were inoculated in an ordered grid pattern on nitrocellulose filters, which were then probed with the osteoarthritis cDNA amplicon ^{32}P-labeled with the Megaprime DNA labeling System (Amersham). The DNA sequence of the non-hybridized recombinants was determined in an Applied Biosystems DNA Sequencer Model 373A or 377 using standard dye terminator chemistry. The seqman module of the Lasergene program (DNAstar) was used for identification of homologous recombinants and grouping them into groups. The Genman module of the Lasergene program was used to search the GenBank databases including the expressed sequence tag database on CDROM. BLAST was used to verify the identification of sequences that showed no homology with entries in the CDROM database.

(Amended) Figure 2 Comparison of the amino acid sequence of human semaphorin III (SEQ ID NO: 13), IV (SEQ ID NO: 11), V (SEQ ID NO: 12), and mouse semaphorin E (SEQ ID NO:9), with the predicted sequence of human semaphorin VI (SEQ ID NO:10). Nucleotide sequence of the cDNA fragment of human semaphorin VI was translated into an amino acid sequence, and compared to that of the corresponding region of human semaphorin III, IV, V and mouse semaphorin E. Conserved amino acids are indicated with boxes. One amino acid gap introduced in the human semaphorin III and V to obtain the best alignment was marked by X.

(Amended) Figure 3 Comparison of amino acid sequence of the human N-acetylglucosamine-6-sulfatase (SEQ ID NO:16) and predicted amino acid sequence from the *C. eleganas* cosmid K09C4 (SEQ ID NO:15) and the

clone ts99 (SEQ ID NO:14). Nucleotide sequence of the cDNA fragment of the clone ts99 was translated to an amino acid sequence, and the corresponding region of the human N-acetylglucosamine-6-sulfatase and C. elegans cosmid K09C4 were compared. Conserved amino acids are marked with boxes.

(Amended) Figure 12 SDF-1 Sequence (SEQ ID NO:17), (SEQ ID NO:18), (SEQ ID NO:19), (SEQ ID NO:20), (SEQ ID NO:21), (SEQ ID NO:22) and (SEQ ID NO:23).